

Serial No.: 09/746,036

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Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A computer-implemented method for analysis analyzing
~~plurality of transcripts in a plurality of samples using a plurality of nucleic acid probe~~
~~arrays comprising:~~
 - a) obtaining a plurality of intensities, each of which reflects the hybridization of
one of a plurality of probes in the a plurality of samples; and
 - b) analyzing the results of nucleic acid probe array based gene expression
experiments for a plurality of transcripts in the plurality of samples using a
plurality of nucleic acid probe arrays by determining the couplings between
the level of the transcript and the intensities, relative transcript levels and
scales of probe arrays by minimizing the effect of cross-hybridization using
linear programming with the constraint that the effect of cross-hybridization is
non-zero.
2. (Currently amended) The method of Claim 1 wherein the minimizing the effect of
cross-hybridization comprises comprising
maximizing $\sum (s(i) + c(j, k) + x(k, l))$ or minimizing
 $\sum (Y(i, j, k, l) - s(i) - c(j, k) - x(k, l))$ with the constraint
 $Y(i, j, k, l) \geq s(i) + c(j, k) + x(k, l)$, wherein $s(i)$ is $\log(\text{scale of probe array})$ for the
 i th probe array, $c(j, k)$ is the $(\log(\text{the coupling between transcript and intensity}))$

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for j th probe and k th transcript, $x(k, l)$ is the *log(relative transcript level)* for the k th transcript in the l th sample, and $Y(i, j, k, l)$ is the *log(I)* for j th probe for k th transcript in the i th probe array hybridized with the l th sample.

3. (Original) The method of Claim 2 wherein $\sum (s(i) + c(j, k) + x(k, l))$ is equivalent to $\sum (s(i) + c(j, k))$ and $\sum x(k, l) = 0$.
4. (Currently amended) The method of Claim 3 wherein the maximizing or minimizing is further constrained by the condition that coupling for perfect match probes is greater than that for mismatch probes.
5. (Original) The method of Claim 4, wherein the scale of probe array is determined independent of the maximizing.
6. (Original) The method of Claim 5 wherein the probe array effect is determined using normalization probes on the probe arrays.
7. (Original) The method of Claim 1 further comprising determining confidence intervals for the relative transcript levels, couplings and scales by bootstrapping on residues, probe arrays or probes.
8. (Currently amended) A system for analysis ~~analyzing plurality of transcripts in a plurality of samples using a plurality of nucleic acid probe arrays comprising:~~

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a processor; and

a memory being coupled with the processor; the memory storing a plurality of machine instructions that cause the processor to perform a plurality of steps when implemented by the processor, the logical steps comprising:

obtaining a plurality of intensities, each of which reflects the hybridization of one of a plurality of probes in ~~the~~ a plurality of samples; and

analyzing the results of nucleic acid probe array based gene expression experiments for a plurality of transcripts in the plurality of samples using a plurality of nucleic acid probe arrays by determining the couplings between the level of the transcript and the intensities, relative transcript levels and scales of probe arrays by minimizing the effect of cross-hybridization using linear programming with the constraint that the effect of cross-hybridization is non-zero.

9. (Currently amended) The system of Claim 8 wherein ~~the~~ minimizing the effect of cross-hybridization comprises comprising

maximizing $\sum (s(i) + c(j, k) + x(k, l))$ or minimizing

$\sum (Y(i, j, k, l) - s(i) - c(j, k) - x(k, l))$ with the constraint

$Y(i, j, k, l) \geq s(i) + c(j, k) + x(k, l)$, wherein $s(i)$ is $\log(\text{scale of probe array})$ for the i th probe array, $c(j, k)$ is the $\log(\text{the coupling between transcript and intensity})$ for j th probe and k th transcript, $x(k, l)$ is the $\log(\text{relative transcript level})$ for the k th transcript in the l th sample, and $Y(i, j, k, l)$ is the $\log(l)$ for j th probe for k th transcript in the i th probe array hybridized with the l th sample.

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10. (Original) The system of Claim 9 wherein $\sum (s(i) + c(j, k) + x(k, l))$ is equivalent to $\sum (s(i) + c(j, k))$ and $\sum x(k, l) = 0$.
11. (Currently amended) The system of Claim 10 wherein the maximizing or minimizing is further constrained by the condition that coupling for perfect match probes is greater than that for mismatch probes.
12. (Original) The system of Claim 11 wherein the scale of probe array is determined independent of the maximizing.
13. (Original) The system of Claim 12 wherein the probe array effect is determined using normalization probes on the probe arrays.
14. (Original) The system of Claim 11 further comprising determining confidence intervals for the relative transcript levels, couplings and scales by bootstrapping on residues, probe arrays or probes.
15. (Currently amended) A computer readable medium having computer executable instructions for performing a method comprising:
obtaining a plurality of intensities, each of which reflects the hybridization of one of a plurality of probes in ~~the~~ a plurality of samples; and
analyzing the results of nucleic acid probe array based gene expression experiments for a plurality of transcripts in the plurality of samples using a

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plurality of nucleic acid probe arrays by determining the couplings between the
level of the transcript and the intensities, relative transcript levels and scales of
probe arrays by minimizing the effect of cross-hybridization using linear
programming with the constraint that the effect of cross-hybridization is non-zero.

16. (Currently amended) The computer readable medium of Claim 15 wherein ~~the~~
minimizing the effect of cross-hybridization comprises comprising

maximizing $\sum (s(i) + c(j, k) + x(k, l))$ or minimizing

$\sum (Y(i, j, k, l) - s(i) - c(j, k) - x(k, l))$ with the constraint

$Y(i, j, k, l) \geq s(i) + c(j, k) + x(k, l)$, wherein $s(i)$ is *log(scale of probe array)* for the
 i th probe array, $c(j, k)$ is the *(log(the coupling between transcript and intensity))*
for j th probe and k th transcript, $x(k, l)$ is the *log(relative transcript level)* for the
 k th transcript in the l th sample, and $Y(i, j, k, l)$ is the *log(I)* for j th probe for k th
transcript in the i th probe array hybridized with the l th sample.

17. (Original) The computer readable medium of Claim 16

wherein $\sum (s(i) + c(j, k) + x(k, l))$ is equivalent to $\sum (s(i) + c(j, k))$ and

$\sum x(k, l) = 0$.

18. (Currently amended) The computer readable medium of Claim 17 wherein the
maximizing or minimizing is further constrained by the condition that coupling for
perfect match probes is greater than that for mismatch prob s.

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19. (Original) The computer readable medium of Claim 17 wherein the scale of probe array is determined independent of the maximizing.
20. (Original) The computer readable medium of Claim 19 wherein the probe array effect is determined using normalization probes on the probe arrays.
21. (Original) The computer readable medium of Claim 20 further comprising determining confidence intervals for the relative transcript levels, couplings and scales by bootstrapping on residues, probe arrays or probes.